Seizures in a 10-week-old infant: lead poisoning from an unexpected source

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A 10-week-old girl was admitted for investigation of seizures and was found to be anemic. Lead poisoning would have been strongly suspected had not the age of the infant and her oral intake (only breast milk and commercial infant formula) made it unlikely.[1,2] This diagnosis, subsequently confirmed by an extremely high blood lead level, was further obscured by a normal blood zinc protoporphyrin level.

We report the case to emphasize three points. Lead encephalopathy must be a major consideration in the diagnosis of unexplained seizures even in very young infants and when there is no obvious source of lead ingestion; the laboratory must be alerted to the possible diagnosis so that an immediate blood lead quantitation can be performed. Although usually elevated in symptomatic chronic lead poisoning the zinc protoporphyrin level in acute or subacute poisoning with a high dose of lead may be normal and thus misleading. Physicians caring for families of middle-Eastern origin must be alert to the potential danger of certain imported utensils.

Case report

The infant was admitted to hospital because of a sudden onset of repeated seizures consisting of stiffening of the body, clonic movements of the left limbs and deviation of the eyes and head to the left. The seizures lasted approximately 10 minutes and were controlled with phenobarbital. The infant appeared otherwise healthy.

This was the first child of parents of middle-Eastern origin. The pregnancy and birth history were unremarkable. The infant's development had been normal, and no regression in milestones had been observed. She had received her first dose of diphtheria toxoid–pertussis vaccine–tetanus toxoid and oral polio vaccine 6 days before admission. She was mildly febrile for about 24 hours but had shown no signs of apathy, lethargy or irritability before the day of admission.

The baby had been breast-fed for 4 weeks and had subsequently received only commercial infant formula. No over-the-counter or unusual medications had been given.

Serum levels of electrolytes, urea, creatinine, calcium, phosphate and magnesium were normal, as were plasma levels of ammonia and lactate, the blood glucose level and the results of liver function tests. A detailed examination of the cerebrospinal fluid was precluded by a traumatic lumbar puncture. Cranial ultrasonography and computed tomography of the head gave normal results. An electroencephalogram was abnormal and showed suppressed background and multifocal sharp wave activity.

There was a normocytic, normochromic anemia with a hemoglobin level of 66 g/L. Coarse basophilic stippling and poikilocytosis were noted in the blood smear. The reticulocyte count was 242 × 10^9/L. The leukocyte and platelet counts were normal.

The bone marrow aspirate showed erythroid hyperplasia and dyserythropoiesis, including coarse basophilic stippling, karyorrhexis and defective hemoglobinization with "veiled" erythroblasts. No nuclear bridging or megaloblastic changes were present.

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The myeloid precursors and megakaryocytes were normal. The iron stores were greater than normal for a child of this age. Numerous pathologic and ringed sideroblasts (16% and 4% of erythroblasts respectively) were also noted. The serum level of iron was 20 (age-specific limits 4 and 18) μmol/L, of transferrin 1.45 (limits 1.43 and 3.47) g/L with a saturation index of 0.6 and of ferritin 197 (normally less than 200) μg/L.

The differential diagnosis included congenital sideroblastic anemia, a variant of congenital dyserythropoietic anemia and lead poisoning. With no apparent source of a toxin the last of these was low on the list, and the blood lead analysis ordered on admission was not an immediate requirement.

The initial blood lead level, reported 5 days after admission, was 7.45 (normally less than 0.72) μmol/L and the zinc protoporphyrin level 49 (normally less than 70) μmol/mol heme. A repeat lead assay, done the next day, resulted in a level of 7.12 μmol/L and an unchanged zinc protoporphyrin level. However, the erythrocyte protoporphyrin concentration in a blood sample taken on admission and assayed later by an extraction method was found to be 13.2 (expected limits 0.18 and 1.0) μmol/L. A radiograph revealed marked lead lines in the long bones. An erythrocyte metabolic profile revealed pyrimidine-5′-nucleotidase activity of 65 (normally 100.5 to 176.1) mU/g hemoglobin.

Chelation therapy was started with dimercaprol and calcium disodium edetate given intramuscularly and intravenously respectively. By the fifth day of treatment the blood lead level had been reduced to 2.36 μmol/L. A second course of chelation therapy was carried out 2 weeks later. Oral treatment with penicillamine was started when the blood lead level was 1.94 μmol/L. After 26 days of therapy the level was 0.77 μmol/L. The zinc protoporphyrin level remained at about 50 μmol/mol heme throughout this time.

The infant, now 14 months old, has no overt signs of neurologic deficit but is being closely monitored by her pediatrician.

Investigation of lead source

The family's country of origin led to initial concern about the use of lead-containing home remedies,[3,4] but no preparations other than formula had been fed to the infant. The source of lead was identified when the parents explained that all the water used to prepare formula had been thoroughly boiled in an electric urn of Iranian origin (Figs. 1 and 2). Inspection of the interior of the urn showed

Fig. 1: Electric urn with identifying markings.

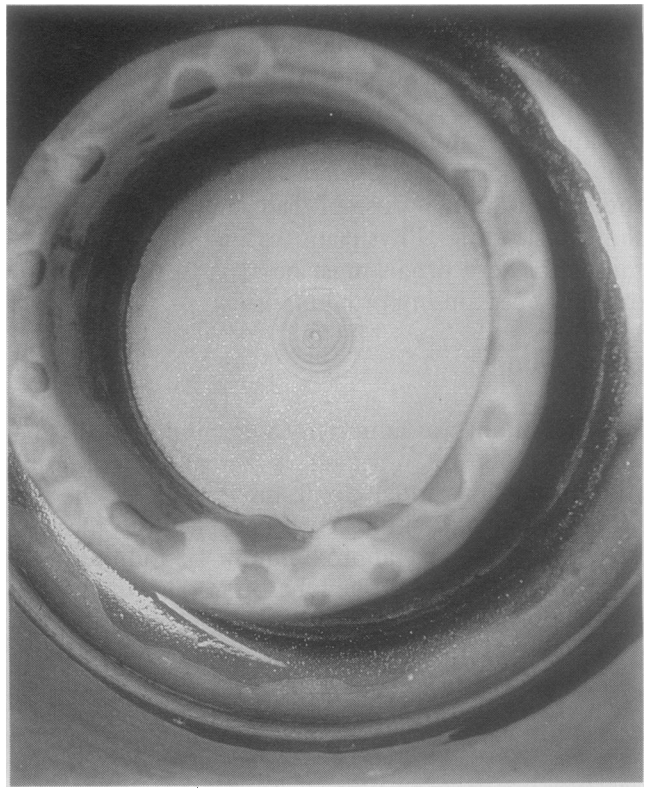

Fig. 2: Interior of urn. Note areas of spot welding and metallic flakes.

obvious areas of spot solder from the original manufacturing process and flecks of metal in the water at the bottom. The parents had not modified the urn in any way since purchase.

Previously boiled tap water from the urn contained 84.94 μmol/L of lead, and deionized water, freshly boiled in the urn, contained 54 μmol/L. The lead content of laboratory tap water ranged from less than 0.001 to 0.19 μmol/L. The parents used water from the same urn to prepare tea. Their blood lead and zinc protoporphyrin levels were 1.12 μmol/L and 47 μmol/mol heme (father) and 1.07 μmol/L and 61 μmol/mol heme (mother).

Enquiries were undertaken to determine whether similar urns were in use in the local community. The urn — apparently a type common in Iran — had been bought from a local store, which had imported only two such urns. The second was located by the father of our patient; it was found to be broken and no longer in use. Water in the base of the second urn also contained a high level of lead.

Methods

Blood, urine and water lead levels were measured by Zeeman graphite furnace atomic absorption spectrophotometry (Varian Canada Inc., Georgetown, Ont.) with ammonium phosphate modifier.[5] The accuracy and precision ratings of our laboratory's whole blood analyses were 96% in the Quebec Interlaboratory Comparison Program.[6] For the blood lead levels our between-run coefficient of variation at 3.70 μmol/L was 2.2% and at 0.23 μmol/L 7.3%. The zinc protoporphyrin level was measured on a hematofluorometer (Helena Laboratories, Beaumont, Tex.). A value of 70 μmol/mol heme is approximately equivalent to 35 μg of total erythrocyte protoporphyrin per decilitre of whole blood.[7] The acid alcohol extraction method measures both free erythrocyte protoporphyrin IX and chelated (zinc) protoporphyrin.[8]

Comments

Lead poisoning from long-term ingestion of lead-based paint is well recognized in the older infant and child.[1,2] Other sources of lead, such as glazes on pottery,[9] flour contaminated by lead-containing mills[10] and oriental cosmetics[11] have also been described. The danger of interior lead solder in electric kettles is known,[12] and Canadian legislation regulates manufacturers to ensure that less than 0.050 parts per million of lead is released into water boiled in these appliances.[13] Therefore, one would not normally consider such water as a likely source of lead contamination.

However, lead encephalopathy in an infant as young as 10 weeks of age requires a search for an extraordinary source of lead. Acute neonatal lead encephalopathy was reported from the United Arab Emirates, where a traditional folk remedy for colic was prepared from powdered rock containing 82.5% lead,[3] and from Saudi Arabia, where a teething powder containing 51% lead was used.[4] No such medication was given to our patient.

In this case the age of the infant and the fact that breast milk and formula were the only oral intake made a diagnosis of lead poisoning unlikely. In reality the infant was being fed a highly concentrated solution of lead: the lead content of the water used to prepare the infant formula was approximately 350 times greater than the current Canadian standard for drinking water (less than 5 μg/dl or 0.24 μmol/L).[14]

The low zinc protoporphyrin level was misleading. This level is increased in iron deficiency and in lead poisoning[15,16] and with the advent of hematofluorometers was recommended as a screen for lead poisoning, particularly in studies involving large samples.[17,18]

In iron-replete states iron is incorporated by the enzyme ferrochelatase into protoporphyrin IX to form hemoglobin. In iron deficiency or inhibition of iron incorporation by chronic lead exposure zinc is chelated into protoporphyrin IX to form zinc protoporphyrin. The ratio of zinc protoporphyrin to free erythrocyte protoporphyrin in these circumstances is about 12:1.[19]

Among rabbits poisoned with lead by weekly intravenous infusion over 4 weeks a massive increase in erythrocyte protoporphyrin was seen.[20] When the total erythrocyte protoporphyrin concentration was less than 200 μg/dl packed cells, 95% was in the form of zinc protoporphyrin. In contrast, when the total erythrocyte protoporphyrin concentration was greater than 1000 μg/dl packed cells only 25% was in the zinc protoporphyrin form, and 75% was unchelated erythrocyte protoporphyrin.[20] As in the rabbit model, our patient received massive amounts of lead over a relatively short time and showed a very high elevation of the total erythrocyte protoporphyrin level, yet the zinc protoporphyrin concentration was not increased. The bone marrow iron stores were increased, and the serum iron and ferritin levels were high. The presence of iron probably inhibited zinc incorporation into protoporphyrin IX.

Lead poisoning must rank high in the differential diagnosis of an unexplained seizure and anemia in any infant, even when no likely source of lead is initially found. Suspicion of lead poisoning demands an immediate blood lead quantitation, and the laboratory must be alerted to minimize the reporting time. A radiograph could rapidly confirm the diag-

nosis. The diagnosis of acute lead poisoning and initiation of chelation therapy must be based on a measurement of the blood lead level, since the results of ancillary tests such as determination of zinc protoporphyrin levels may be misleadingly normal in subacute massive lead poisoning.

Addendum

After this paper was accepted for publication a second infant was admitted with lead poisoning from water boiled in an Iranian stove-top kettle (Fig. 3). The kettle water had been used for 3 months to prepare infant formula and cereal. This 7-month-old boy presented with severe vomiting, listlessness, apathy and pallor. The blood lead level on admission was 15.62 μmol/L and the zinc protoporphyrin level 154 μmol/mol heme.

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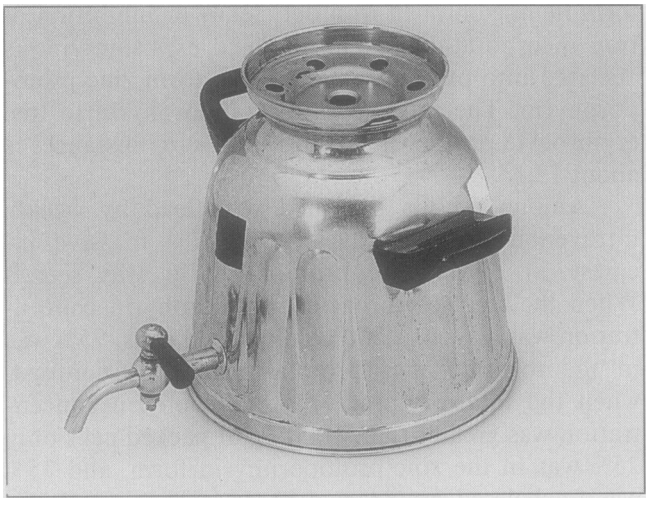

Fig. 3: Stove-top kettle implicated in second case.

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